

CORRECTED VERSION

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Organization
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(43) International Publication Date
29 April 2004 (29.04.2004)

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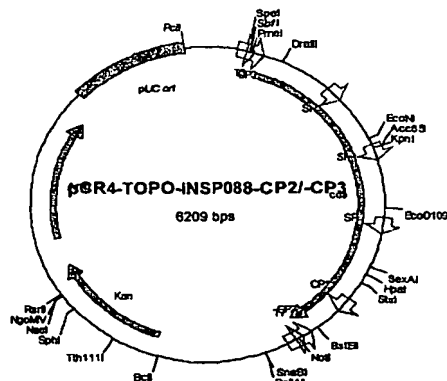
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 (30) Priority Data:
 0224116.4 16 October 2002 (16.10.2002) GB
 (71) Applicant (*for all designated States except US*): INPHARMATICA LIMITED [GB/GB]; 60 Charlotte Street, London W1T 2NU (GB).
 (72) Inventors; and
 (75) Inventors/Applicants (*for US only*): FAGAN, Richard, Joseph [US/GB]; Inpharmatica Limited, 60 Charlotte Street, London W1T 2NU (GB). PHELPS, Christopher, Benjamin [GB/GB]; Inpharmatica Limited, 60 Charlotte Street, London W1T 2NU (GB). RODRIGUES, Tania, Maria [PT/GB]; Inpharmatica Limited, 60 Charlotte Street, London W1T 2NU (GB). POWER, Christine [GB/FR]; 10, rue des Jonquilles, F-01710 Thoiry (FR). BIENKOWSKA, Jadwiga [PL/US]; 45 Fayette St. Apt.3, Cambridge, MA 02139 (US).
 (74) Agents: GOODFELLOW, Hugh, Robin et al.; Carpmaels & Ransford, 43-45 Bloomsbury Square, London WC1A 2RA (GB).
 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,

[Continued on next page]

(54) Title: ALPHA MACROGLOBULIN FAMILY MEMBERS

Molecule: pCR4-TOPO-INSP088-CP2/-CP3, 6209 bps DNA Circular				
Type	Start	End	Name	Description
MARKER	205		M13R	M13 rev priming site
MARKER	243		T3	T3 priming site
REGION	295	2546	Insert	
MARKER	295		CP3	INSP088-CP3 cloning primer
GENE	336	2531	cds	INSP088 mactroglobulin domain cds
MARKER	794		SP1	INSP088-SP1 sequencing primer
MARKER	1221		SP2	INSP088-SP2 sequencing primer
MARKER	1689		SP3	INSP088-SP3 sequencing primer
MARKER	2240		CP1	INSP088-CP1 amplification primer
MARKER	2527	C	CP2	INSP088-CP2 cloning primer
MARKER	2532		stop	INSP088 stop codon
MARKER	2580	C	T7	T7 priming site
MARKER	2607	C	M13F	M13 for priming site
GENE	3411	4205	Kan	Kanamycin resistance gene ORF
GENE	4409	5269	Amp	Ampicillin resistance gene ORF
REGION	5414	6087	pUC ori	pUC origin



(57) Abstract: This invention relates to two proteins, termed INSP087, herein identified as members of the alpha macroglobulin family, in particular as alpha-2-macroglobulin-like proteinase inhibitors, and to the use of these proteins and nucleic acid sequences from the encoding genes in the diagnosis, prevention and treatment of disease.

WO 2004/035626 A2



KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: ALPHA MACROGLOBULIN PROTEIN FAMILY MEMBERS

(57) Abstract: This invention relates to two proteins, termed INSP087, herein identified as members of the alpha macroglobulin family, in particular as alpha-2-macroglobulin-like proteinase inhibitors, and to the use of these proteins and nucleic acid sequences from the encoding genes in the diagnosis, prevention and treatment of disease.

WO 2004/035626 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/04500

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/81 C12N15/15

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBL, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 91/03557 A (NOVONORDISK AS) 21 March 1991 (1991-03-21) page 11, line 18 - line 30 page 32, line 35 - line 38 pages 34 to 41, SEQ ID NO:1 -----	1-3, 7-17, 19, 23-49
X	DATABASE EMBL 'Online! 13 February 2002 (2002-02-13), "Novel human diagnostic protein #5706" XP002275606 retrieved from EBI Database accession no. ABG05715	1-3, 7-17, 19, 23-49
X	-& WO 01/75067 A (HYSEQ INC ; LIU CHENGHUA (US); TANG Y TOM (US); DRMANAC RODOJE T (U) 11 October 2001 (2001-10-11) page 101; claim 20 ----- -/--	1-3, 7-17, 19, 23-49

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the international search

31 March 2004

Date of mailing of the international search report

17. 08. 2004

Name and mailing address of the ISA

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Grötzinger, T

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/04500

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! 13 February 2002 (2002-02-13), "DNA encoding novel human diagnostic protein #5706" XP002275607 retrieved from EBI Database accession no. AAS69902</p>	<p>1-3, 7-17, 19, 23-49</p>
X	<p>-& WO 01/75067 A (HYSEQ INC ;LIU CHENGHUA (US); TANG Y TOM (US); DRMANAC RODOJE T (U) 11 October 2001 (2001-10-11) page 99; claim 1</p>	<p>1-3, 7-17, 19, 23-49</p>
X	<p>----- KAN C-C ET AL: "NUCLEOTIDE SEQUENCE OF CDNA ENCODING HUMAN ALPHA2-MACROGLOBULIN AND ASSIGNMENT OF THE CHROMOSOMAL LOCUS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 82, no. 8, April 1985 (1985-04), pages 2282-2286, XP001038062 ISSN: 0027-8424 abstract page 2284; figure 1</p>	<p>1-3, 7-17, 19, 23-49</p>
X	<p>----- DEVRIENDT K ET AL: "PRIMARY STRUCTURE OF PREGNANCY ZONE PROTEIN MOLECULAR CLONING OF A FULL-LENGTH PZP COMPLEMENTARY DNA CLONE BY THE POLYMERASE CHAIN REACTION" BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1088, no. 1, 1991, pages 95-103, XP009028652 ISSN: 0006-3002 abstract page 99; figure 4</p> <p>-----</p>	<p>1-3, 7-17, 19, 23-49</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/04500

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 18, 20-22
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-3, 7-17 (partially), 19 (partially), 23-49 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ GB 03 /04500

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 24, 29, and 42 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound.

Claims 34 and 39 are directed to a method of treatment of the human/animal body. Again, the search has been carried out and based on the alleged effects of the compound.

Continuation of Box I.2

Claims Nos.: 18, 20-22

Present claims 18, and 20 to 22 relate to an extremely large number of possible ligands/compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the ligands/compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the ligands/compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely antibodies directed against the protein of the application.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ GB 03/ 04500

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1 to 3, 7 to 17 (partially), 19 (partially), 23 to 49 (partially)

Protein "INSP087", polynucleotides encoding the protein, vectors, host cells, antibodies, medical uses, diagnostic methods, pharmaceutical compositions, vaccines, kits, and transgenic or knock-out non-human animals.

2. claims: 4 to 6, 7 to 17 (partially), 19 (partially), 23 to 49 (partially)

Protein "INSP088", polynucleotides encoding the protein, vectors, host cells, antibodies, medical uses, diagnostic methods, pharmaceutical compositions, vaccines, kits, and transgenic or knock-out non-human animals.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 03/04500

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9103557	A	21-03-1991	AU 6357890 A	08-04-1991
			WO 9103557 A1	21-03-1991
			EP 0489830 A1	17-06-1992
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			US 2002061567 A1	23-05-2002
			US 2003180722 A1	25-09-2003
			US 2002146757 A1	10-10-2002